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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,069	05/31/2001	Joseph Hamburger	01/22115	9244

7590 03/25/2004
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EXAMINER

CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/857,069

Applicant(s)

HAMBURGER ET AL.

Examiner

Shin-Lin Chen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 January 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 53-63 and 65-69 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 53-63 and 65-69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed 1-21-04 has been entered. Claims 53, 54, 59, 60, 63 and 65-69 have been amended. Claim 64 has been canceled. Claims 53-63 and 65-69 are pending and under consideration.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 53-55, 63 and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Rushforth et al., 1989, Abstract No. 223 at 1989 International Worm Meeting. Applicants' amendment filed 1-21-04 necessitates this new ground of rejection.

Claims 53-55, 63 and 65 are directed to a method of genetically modifying a multicellular eukaryotic diploid parasite, such as flat worm, by transforming a multicellular-differentiated developmental stage of the multicellular eukaryotic diploid parasite using biolistic bombardment. Claim 63 specifies said parasite is sensitive to a known drug. Claim 65 specifies a transgene integrated in the genome of the parasite.

Rushforth teaches using particle acceleration of microprojectiles coated with plasmid DNA to introduce transforming DNA into *C. elegans* and recovers both transient and heritable transformants. The plasmid DNA is dried onto the surfaces of gold particles and about 70,000 plasmid DNA molecules are coated per particle. Rushforth also teaches that the *C. elegans* are

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collected by filtration on Millipore filters, briefly air dried and mounted onto chilled plates containing isotonic recovery buffer solidified with agar and the transformants are heritable for many generations. The transformants are heritable for many generations which implies that they are stable transformants although the frequency of obtaining heritable transformants is low. It is inherent that *C. elegans* is sensitive to a known drug. Thus, claims 53-55, 63 and 65 are anticipated by Rushforth.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 53-63 and 65-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller, 1997 (WO 97/11191) in view of Rushforth et al., 1989, Abstract No. 223 at 1989

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International Worm Meeting. Applicants' amendment filed 1-21-04 necessitates this new ground of rejection.

Claims 53-63 and 65-69 are directed to a method of genetically modifying a multicellular eukaryotic diploid parasite, such as a flat worm schistosome, comprising direct transforming said parasite with a transformation method, such as biolistic bombardment. Claim 63 specifies the parasite is sensitive to a known drug. Claims 67 and 68 specify the selected genomic locus is a repetitive sequence or a unique sequence. Claim 69 specifies the parasite has distinguishable sexes.

Miller teaches a method of generating genetically engineered schistosome as an intermediate vector for secretion of desired protein, such as therapeutic protein, into the bloodstream of humans and other susceptible hosts via microinjection of the transgene DNA into the pronuclei or cytoplasm of the zygotes of stage I schistosome eggs. "The use of schistosomes as intermediate vector facilitates mass production, quality control, termination of therapy at will and dose titration" (e.g. abstract, p. 38). Miller teaches there are male and female schistosome worms (e.g. p. 6-8).

Miller does not teach using biolistic particle bombardment to generate genetically modified schistosome or diploid parasites. Miller does not specifically teach the selected genomic locus is a repetitive locus or a unique sequence.

Rushforth teaches using particle acceleration of microprojectiles coated with plasmid DNA to introduce transforming DNA into *C. elegans* and recovers both transient and heritable transformants. The plasmid DNA is dried onto the surfaces of gold particles and about 70,000 plasmid DNA molecules are coated per particle. Rushforth also teaches that the *C. elegans* are

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collected by filtration on Millipore filters, briefly air dried and mounted onto chilled plates containing isotonic recovery buffer solidified with agar and the transformants are heritable for many generations. The transformants are heritable for many generations which implies that they are stable transformants although the frequency of obtaining heritable transformants is low.

It would have been obvious for one of ordinary skill at the time of the invention to substitute the microinjection method as taught by Miller with the ballistic bombardment with microprojectiles coated with nucleic acids as taught by Rushforth for stable transformation of a diploid parasite, such as a schistosome, with a vector containing desired DNA sequence because both schistosome and *C. elegans* are multicellular parasites and it was well known in the art at the time of the invention to use ballistic bombardment for stable transformation of animal cells and to make genetically modified animal including parasites. Random integration of genome via microinjection or site-directed homologous recombination into genome can target repetitive sequences or unique sequences in the genome and those techniques were well known in the art at the time of the invention. Therefore, it would have been obvious for one of ordinary skill at the time of the invention to target a selected genomic locus, either repetitive locus or unique sequences.

One having ordinary skill at the time the invention was made would have been motivated to do so in order to use schistosome as intermediate vector for secretion of desired protein, such as therapeutic protein, into the bloodstream of humans and other susceptible hosts and to facilitate mass production, quality control, termination of therapy at will and dose titration as taught by Miller or to generate genetically modified *C. elegans* as taught by Rushforth with reasonable expectation of success.

Conclusion

No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for this group is (703) 872-9306.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.

A handwritten signature in black ink, appearing to read 'S L Chen'.